

AMENDMENT TO THE CLAIMS

A listing of the claims presented in this patent application appears below. This listing replaces all prior versions and listing of claims in this patent application.

Claim 1 (currently amended): A method of identifying a compound which modulates binding of a ~~natural~~ ligand selected from the group consisting of EGF, heparin-binding EGF, TGF α , vaccinia virus growth factor, betacellulin and amphiregulin to the EGF receptor, ~~ErbB3 or ErbB4[[],]~~ or which modulates signal transduction ~~via by binding to~~ the EGF receptor, ~~ErbB2, ErbB3 or ErbB4[[],]~~ which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and ~~the a~~ molecule, wherein the molecule comprises:

- (i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6; or
- (ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations;

~~(iii) amino acids present in the amino acid sequence of ErbB2, ErbB3 or ErbB4, which form an equivalent three dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;~~

(B) ~~obtaining selecting~~ a compound assessed in step (A) which possesses stereochemical complementarity to the molecule; ~~and~~

(C) testing the compound in vivo or in vitro for its ability to

- (i) modulate binding of a ~~natural~~ ligand selected from the group consisting of EGF, heparin-binding EGF, TGF α , vaccinia virus growth factor, betacellulin and amphiregulin to the EGF receptor, ~~ErbB3 or ErbB4[[],]~~ or
- (ii) modulate signal transduction ~~via by binding to~~ the EGF receptor~~[[],]~~ ~~ErbB2, ErbB3 or ErbB4[[],]~~; ~~and~~

- (D) selecting and obtaining a compound tested in step (C) that has the ability to
- (i) modulate binding of a ligand selected from the group consisting of EGF, heparin-binding EGF, TGF α , vaccinia virus growth factor, betacellulin and amphiregulin to the EGF receptor, or
 - (ii) modulate signal transduction by binding to the EGF receptor.

Claims 2 - 53 (canceled).

Claim 54 (previously added): The method according to claim 1, wherein the testing in (C) is carried out *in vitro*.

Claim 55 (previously added): The method according to claim 54, wherein the testing is performed by a high throughput assay.

Claim 56 (previously added): The method according to claim 1, wherein the testing in (C) is carried out *in vivo*.

Claim 57 (previously added): The method of claim 1, in which step (C)(ii) involves testing the compound for the ability to modulate EGF receptor mediated cell proliferation.

Claim 58 (currently amended): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 313-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 59 (canceled).

Claim 60 (currently amended): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) is defined by amino acids 1-475 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6.

Claim 61 (canceled).

Claim 62 (canceled).

Claim 63 (previously added): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the β -sheet of the L1 domain of the EGF receptor.

Claim 64 (canceled).

Claim 65 (previously added): The method of claim 1, wherein the one or more subsets of amino acids in step (A)(ii) are the amino acids that form the β -sheet of the L2 domain of the EGF receptor.

Claim 66 (canceled).

Claim 67 (currently amended): The method of claim 1, which further includes the step of modifying the compound selected in step (B) or step (D) such that to enhance binding to a lower face containing the second β -sheet of the L1 and/or L2 domains is enhanced in the modified compound compared to the unmodified compound, wherein the structure of the face is characterized by a plurality of solvent-exposed hydrophobic residues.

Claim 68 (previously added): The method of claim 67, in which the hydrophobic residues include:

- (i) Tyr64, Leu66, Tyr89, Tyr93; and/or
- (ii) Leu348, Phe380 and Phe412.

Claim 69 (previously added): The method of claim 1 in which the compound is identified from test compounds in a database.

Claim 70 (currently amended): The method of claim 1, which further includes the step of selecting a compound that increases signal transduction *via* by binding to the EGF receptor~~[,] ErbB2, ErbB3 or ErbB4~~.

Claim 71 (currently amended): The method of claim 1, which further includes the step of selecting a compound that decreases signal transduction *via* by binding to the EGF receptor~~[,] ErbB2, ErbB3 or ErbB4~~.

Claim 72 (currently amended): The method of claim 1, which further includes the step of selecting a compound that inhibits or prevents the binding of a ligand selected from the group consisting of EGF, heparin-binding EGF, TGF α , vaccinia virus growth factor, betacellulin and amphiregulin natural ligand to the EGF receptor~~[,] ErbB3 or ErbB4~~.

Claim 73 (currently amended): A method of identifying a compound which binds to a ~~molecule of the EGF receptor family selected form the group consisting of~~ the EGF receptor, ~~ErbB2, ErbB3 and ErbB4~~~~[,]~~ which method comprises the steps of:

(A) assessing the stereochemical complementarity between the compound and the molecule, wherein the molecule comprises:

- (i) amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6; or

- (ii) one or more subsets of said amino acids related to the coordinates shown in Figure 6 by whole body translations and/or rotations; or
 - (iii) ~~amino acids present in the amino acid sequence of ErbB2, ErbB3 or ErbB4, which form an equivalent three dimensional structure to that of the receptor site defined by amino acids 1-621 of the EGF receptor positioned at atomic coordinates substantially as shown in Figure 6;~~
- (B) ~~obtaining one ore more compounds which possesses stereochemical complementarity to the molecule~~ selecting a compound assessed in step (A) which possesses stereochemical complementarity to the molecule; and
- (C) selecting a compound from step B that has [[a]] an experimentally determined K_d or K_I of less than 10^{-6} M for ~~a molecule of the EGF receptor family selected from the group consisting of the EGF receptor[[],] ErbB2, ErbB3 and ErbB4.~~

Claim 74 (previously added): A method as claimed in claim 73, wherein K_d is less than 10^{-8} M.

Claim 75 (previously added): The method of claim 73, wherein K_I is less than 10^{-8} M.